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SEGMENTATION AND FRAGMENTATION OF THE MYOCARDIUM.[1]

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THE muscular fibres of the mammalian heart were shown by Eberth[2] to be columns of short striated and nucleated cells or segments held together at the ends by a delicate cement. The cells have lateral processes that coalesce, by means of cement, with those of adjacent cells. Normally the layers of cement between the ends of the cells and their processes are not visible; on the addition of acetic acid the cement substance becomes quite plain, and with 30 per cent. solution of caustic potash the individual muscle-cells may be isolated (segments of Weissmann).

Of the morbid changes of the myocardium proper none occur more frequently or under a greater variety of circumstances than the lesion known as segmentation[3] and fragmentation of the muscle-fibres.

While Virchow,[4] v. Zenker,[5] Rindfleisch,[6] and Coats[7] make incidental mention of transverse separation or fracture of the cardiac muscle-fibres, Renaut,[8] in association with Landouzy, in 1877, was the first to call direct attention to the dissociation of the muscle-cells. They showed that, as they believed, under the influence of general nutritive disturbances the intercellular cement softened and the individual cells were set free. They referred to this condition as "disintegration, dissociation, segmentation—*état segmentaire.*" This observation was followed by a number of

[1] Read before the Philadelphia Pathological Society, April 22, 1897.

[2] Die Elemente der Guergestreiften Muskeln, Virchow's Archiv, 1866, Bd. xxviii. p. 100.

[3] In biology segmentation means cell-cleavage; generally it means the act of dividing into the segments or parts into which any body naturally separates. It is in the latter sense that the word is used in connection with the lesions of the myocardium under discussion, and it means the separation of the muscle-fibres of the heart into the cells or segments of which they are composed. "Fragmentation" signifies a breaking into irregular pieces. Both terms are applied to dissociation of the cardiac muscle fibres. In this paper they will be employed as consistently as possible.

[4] Ueber parenchymatöse Entzündung, Virch. Arch., Bd. iv. p. 266.

[5] Ueber die Veränderungen der willkürlichen Muskeln in Typhus Abdominalis, 1864.

[6] Lehrbuch der pathologischen Gewebelehre, 1870, p. 202; 4th ed., p. 239.

[7] Two Cases of Calcareous Infiltration of the Muscular Fibres of the Heart, Glasgow Medical Journal, 1872.

[8] Note sur les alterations du myocarde accompagnant l'inertie cardiaque, Société de Biologie, July 7, 1877.

clinical and anatomical studies of the subject by pupils of Renaut as well as by other French writers—Colrat,[1] Durand,[2] Chalot,[3] Weill,[4] Dejerine,[5] Duplaix,[6] Mollard.[7] Mention of the change was also soon made by various French systematic writers—Pitres,[8] Lancereaux,[9] Jaccard,[10] Paul,[11] Robin,[12]—and in 1890 Renaut[13] published an article in which he not only describes the anatomical changes, but also gives the clinical picture of the condition, which he dignifies as an independent disease. The principal symptoms are: Arhythmia, weakening of the impulse of the apex, some increase in the area of the heart's dulness, an uncertain systolic murmur, and, occasionally, œdema of the lower extremities. He attributes the dissociation of the cells to solution of the cement substance on account of senile involutionary changes, alcoholism, infection, and the associated high temperature. Individuals affected with such changes in the heart-muscle may perish on account of syncope or asystole, or from intercurrent diseases which, otherwise of little importance, assume a much more serious aspect on account of the existing heart-lesion.

In 1888 Przewoski and Klein[14] described some cases of very sudden death which were attributed to extensive myocardial segmentation. The following year Browicz[15] published a study of segmentation based on the careful examination of forty-two cases. This is the first publication on the subject in the German language. He concludes that segmentation is due to changes in the cement substance, occurs ante mortem, and may cause cardiac insufficiency and arrest of the heart's action.

In the discussion upon the disturbances of the myocardium at the Tenth International Medical Congress in Berlin, in 1890, v. Recklinghausen[16] states that microscopic appearances and the frequent connection of dissociation with sudden or rapid, spontaneous death lead him to regard this change in the cardiac fibres as the result of excessive stimulation

[1] Contribution a l'étude des myocardites chroniques et la désintegration cardiaque, Lyon Méd., 1879.

[2] Etude anatomique sur la segment cellulaire cardiaque, Thèse de Lyon, 1879.

[3] Essai sur la désintegration de la fibre musculaire, Thèse de Paris, 1880.

[4] De la mort subite dans la pleurésie, Revue de Médecine, 1887, No. 1.

[5] Sur les altérations du myocarde come cause de mort subite dans le fièvre typhoide, Soc. de Biol., Dec. 26, 1885.

[6] Contribution a l'étude de la sclerose, Arch. Gén. de Médecine, 1885, 7 série, p. 145.

[7] De la myocardite sigmentaire essentielle et principalement de la forme senile de cette affection, Thèse de Lyon, 1889.

[8] Des hypertrophies et des dilatations cardiaques indépendantes des lésions valvulaires, 1878.

[9] Traité d'anat. path., 1881, p. 799.

[10] Traité de path. interne, 1883.

[11] Maladies du coeur, 1883, p. 468.

[12] Leçons de clinique et thérapeutique médicale, 1877, 20 ième leçon.

[13] Gazette des Hôpitaux, 1890, p. 202.

[14] Gazeta lekarska, 1888, No. 18.

[15] Ueber das Verhalten der Muskelzellbalken des Herzens in path. Zuständen, Wiener kl. Wochenschrift, 1890, No. 80.

[16] Verhandlungen des X Intern. med. Congress, Berlin, 1890, Bd. ii. Abth. 3.

and irregular contraction of their substance, which passes directly into rigor mortis, and is accompanied with a separation into segments as well as a breaking into fragments. There is, therefore, no ground for believing, as Renaut does, that the primary change is in the cement substance. The frequent association of these changes with the various pathological conditions included under the term myocarditis shows that these conditions, on account of changes in the muscular tissue or in the heart's activity, predispose the fibres to dissociation.

v. Zenker[1] agrees as to the agonal character of actual dissociation. It would be impossible for cardiac contractions to continue after a general disintegration in this manner of the muscle-fibres; but it is equally evident that a heart whose fibres undergo agonal dissociation must have been the seat of intravital, physical, and chemical changes that gave rise to the weakness and final arrest. The *état segmentaire* is, therefore, an anatomical change that explains to a certain extent many deaths from "heart-failure" (*Herzschlag*).

Marchand[2] (Marburg) in the same discussion questions the statement that the fragments always correspond to the heart muscle-cells, and suggests that possibly the lines of separation represent, as assumed by Wagner, irregular lines of contraction along which separation later on occurs.

Tedeschi[3] found that in two hundred and thirty-six deaths from various causes segmentation was present in 48 per cent. The frequency of dissociation in infectious diseases and in acute and chronic diseases of the central nervous system lead this author to believe that physical changes in the cement, due to toxic substances or to nutritive disturbances, are the essential causes of the process.

Israel[4] made the important observation that in districts of separation there is a marked loosening in the secondary bundles, due apparently to stretching of the intermuscular connective tissue—a change that would point to the action of mechanical influences. Not being able to produce any changes by means of mechanical overdilatation or stretching of dead hearts, he assumes the constant presence of some deviation from the normal in the primitive bundles of disunited hearts, such as pigment atrophy, parenchymatous changes, and fatty degeneration. Under such conditions he is inclined to conclude that any increase in the work placed upon the heart may lead to separation.

Oestreich,[5] in 1894, reviewed dissociation or fragmentation with reference to the anatomical changes, to its relation to the cement, and to its importance as regards the heart's work. He came to the conclusion that it concerns not so much separation of the muscle-fibres into muscle-

[1] Loc. cit. [2] Loc. cit.
[3] Ueber die Fragmentatio des Myocardium, Virch. Arch., 1892, Bd. cxxviii. p. 185.
[4] Zur Entstehung der Fragmentatio Myocardii, Virch. Arch., 1893, Bd. cxxxiii. p. 551.
[5] Die Fragmentatio Myocardii, Virch. Arch., 1894, Bd. cxxxv. p. 79.

cells by a solution of the cement, as spoken of by the previous authors, but that fragmentation is essentially, as this term would imply, multiple fractures or tears of muscle-fibres, the lines of which oftener pass through the muscle-cells than along the cement substance. Longitudinal ruptures were also occasionally seen. Such being the case, and fragmentation occurring very often in otherwise normal hearts in persons dying suddenly, rapidly, or slowly from known causes, he concludes that it is caused by irregular contractions during the death agony, and may occur in connection with practically all diseases and modes of death.

L. Bard[1] regards the *état segmentaire* of Renaut as fragmentation or rupture of the fibres rather than a segmentary dissociation. These ruptures are probably of post-mortem origin, due to reagents and diverse manipulations; yet they are not artefacts, because the real condition is an excessive fragility on account of secondary nutritive troubles. It is, therefore, a subordinate lesion, found in grave acute diseases and in asystolic hearts, that cannot be promoted to the rank of a special primary process.

Renaut,[2] at the first French Congress of Medicine, in 1894, again reviews the subject of segmentary dissociation of the myocardium, and essays to prove, in contradiction to v. Recklinghausen,[3] Oestreich,[4] and others, that it concerns an undoubtedly vital and not merely agonal lesion; that segmentation and fragmentation are part and parcel of a complex and progressive, definite, morbid process, the seat of which is in the muscle-cells. This process is characterized anatomically by great swelling or gigantism of the nuclei of the muscle-cells, by a marked increase of the intercontractile plasma of the cells, which causes an atrophy of the fibrillæ—"hyperplasmic atrophy"—making the fibres perhaps brittle, and thus predisposing to fragmentation; and, finally, by softening and liquefaction of the intercellular cement, which allows segmentation to take place. This dystrophy, of whatever cause it may be, leads sooner or later to cardiac asthenia, and Renaut claims that senile cardiac insufficiency due to this pathological process is susceptible of clinical diagnosis.

American medical literature is silent upon the subject of myocardial dissociation. The scattered remarks on the subject in the *Twentieth Century Practice* contain historically erroneous statements that deprive Renaut of his due credit as the one to whom we owe our knowledge of the lesion.

The essential basis for the present consideration of this form or forms of disturbance in the myocardium rests partly upon a study of the litera-

[1] De la signification anatomique et clinique des diverses lésions du myocard, Congrès Français de Médecine (1894), Paris, 1895, p. 806.

[2] Sur la dissociation segmentaire du myocarde, Congrès Français, etc., 1895.

[3] Loc. cit. [4] Loc. cit.

ture bearing on the subject, but essentially upon the results obtained from investigation of a large number of hearts from animals and human beings dying from a variety of causes and under diverse circumstances.

ARTIFICIAL SEGMENTATION. The authors are now practically agreed that segmentary dissociation is not of post-mortem origin, neither is it an artefact. v. Recklinghausen,[1] Renaut,[2] and others have found well-marked segmentation in hearts from bodies—especially of executed individuals—that were examined immediately after death. I have found it present in bodies examined within one hour after death.

Histologists are well aware, especially since Eberth's[3] work, that certain reagents, such as solutions of acetic acid, have to be applied to render the cement substance visible; and, furthermore, that 30 or 40 per cent. solutions of KOH dissolve the cement and set the muscle-cells free.

Tedeschi[4] found that the fixing and staining fluids ordinarily in use do not produce misleading artefacts. Flemming's solution only seemed to render the cement substance visible, and should consequently not be used in studying the heart-muscle in regard to the presence of segmentation.

While segmentation was looked upon as a cadaveric change by O. Israel,[5] in 1889, he freely denies all influence of artificial and post-mortem factors in its production in 1893.[6]

Rindfleisch claims to have produced mechanical disintegration by overdistention of a dead rabbit's heart, but neither Israel[7] nor Browicz[8] could produce segmentation by mechanical overdilatation and stretching of dead hearts. Israel[9] found that forcible overdilatation of tetanized hearts did not produce dissociation.

While decomposition under ordinary circumstances (Browicz,[10] Tedeschi[11]) does not cause dissociation, Dunin[12] found that artificial gastric juice as well as decomposition under water may cause separation of the cells. He, therefore, regards chemical changes in the organism as the essential cause of dissociation, while mechanical conditions might produce ruptures of the muscle-cells themselves. He expresses the opinion that possibly the agonal invasion of the bacterium coli commune may cause chemical solution of the cement substance.

A number of human hearts were allowed to decompose in a moist atmosphere, at room temperature as well as in the ice-box; but it so happened that none of them, examined at irregular intervals up to ten

[1] Loc. cit. [2] Loc. cit. [3] Loc. cit. [4] Loc. cit.
[5] Praktikum der path. Histologie, 1889, p. 255. [6] Loc. cit. [7] Loc. cit.
[8] Ueber d. Bedutlung d. Veränderungen der Kittsubstanz der Muskelzellbalken des Herzens, Virch. Arch., Bd. cxxxiv. p. 1.
[9] Loc. cit. [10] Loc. cit. [11] Loc. cit.
[12] Einige Bemerkungen über der Fragmentation der Herzmuskelzellen, Ziegler's Beiträge, 1894, Bd. xvi.

days after removal from the body, showed any separation of the fibres. Pieces from healthy human hearts were also allowed to decompose under water as well as to remain for from twenty-four to forty-eight hours in bouillon cultures of colon bacilli; but the fibres did not become disunited, not even in the vicinity of the bacterial colonies in the interior of the pieces. Similar results were obtained with animal hearts. In this respect my observations differ from those reported by Dunin.

Animal as well as human hearts were examined before and after rigor mortis, but no difference in the structure of the muscle-fibre was observed. Hearts were allowed to freeze stiff, but segmentation did not occur. The view expressed by Rosenbach,[1] that the fall of the temperature of the body after death leads to dissociation, did not receive support.

It may, therefore, be concluded that true segmentation, as ordinarily observed, is not an artefact or post-mortem change. In reality there is all reason to believe that no artificial separation of the cells can, under any circumstances, present such microscopic pictures as the sections of hardened specimens of hearts the seat of typical dissociation (Fig. 5). On the other hand, it cannot be denied that various reagents and manipulations may produce ruptures of the muscle-fibres, especially if the latter are brittle on account of degenerative changes. Thus, pressure on the cover-glass may be sufficient to produce breaks in underlying fibres in teased and unimbedded specimens.

Experimental Segmentation and Segmentation in Animals. Tedeschi[2] instituted an extensive series of experiments; but infections, injuries to the brain, traumatic sudden death, overstimulation, etc., failed to produce dissociation in mice, guinea-pigs, rabbits, cats, and dogs. Cutting of the vagus produced indications of segmentation in circumscribed districts. Some segmentation also occurred around wounds made with red-hot needles.

Oestreich,[3] having observed segmentation in persons that died from or in chloroform narcosis, tried in vain to produce this change by killing animals (four dogs and one rabbit) by administration of chloroform.

Charrin[4] showed that among the extensive changes in the myocardium following the injection of the sterile products of the bacillus pyocyaneus are necrotic areas, in the centre of which there may be segmentation of the fibres.

J. Mollard and Cl. Regnaud[5] found that in dogs that die from diphtheria intoxication sinuous lines corresponding to the points of contact of the muscle-cells at times become visible, and that occasional segmentation may take place. Fractures of the fibres were also present.

[1] Die Krankheiten des Herzens und ihre Behandlung, p. 666. [2] Loc. cit.
[3] Loc. cit. [4] Verh. d. X. Intern. Med. Congresses, 1890, Bd. ii. Abth. 2.
[5] Lésions du myocarde dans l'intoxication aigue par la toxine diphthérique, Annales d. l'institut Pasteur, 1897, t. ii. p. 97.

I have examined a large number of hearts from dogs, cats, chickens, rabbits, guinea-pigs, mice, and rats that died from various infections or were killed in the course of ordinary laboratory experiments (here is included a number of animals that died from experimental air embolism). The results were practically negative as regards segmentation. Only in one guinea-pig that died from diphtheria intoxication did the heart present distinctly visible transverse cement lines.

The fresh hearts were obtained from six hogs, six sheep, and six young cattle butchered at the stock-yards. Segmentation was not present in a single heart; not even were the cement lines visible. All the hearts were firm and healthy.

A thorough histological study was also made of the different portions of ten horse hearts. The hearts were obtained from old and useless horses that were killed for the products obtainable from their bodies. In almost all these hearts the cement substance was quite distinct, in the form of transverse, quite straight, more or less prominent lines; but typical segmentation was not observed in a single instance. The pigment was very plain in some of these specimens.

Through the courtesy of Dr. A. H. Baker, of the Chicago Veterinary College, I obtained the heart of a horse that died of enteritis and the heart of one dying from influenza, pneumonia, and exudative pleurisy. Both these hearts were the seat of well-marked parenchymatous degeneration, the consistence being rather soft and the cut surface presenting a yellowish-gray, opaque appearance, and the sections showed some separation of the muscular fibres in the right as well as in the left ventricle, but this separation seemed to be due more to a rupture of the fibres than to solution of the cement, because the margins of the fragments were very ragged.

It is consequently probable that in the hearts of diseased larger animals segmentation and fragmentation also occur, although perhaps not to such an extent as these changes are observed in man. It would seem that, on the whole, human heart-muscle is especially prone to dissociation as compared with the heart-muscle of animals.

Segmentation and Fragmentation in Man. The hearts from more than two hundred persons dying from all sorts of causes have been studied as regards segmentation and allied changes. Many of these hearts were obtained through the courtesy of Dr. Louis J. Mitchell, physician to the Coroner's office of Cook County, and I wish to thank Dr. Mitchell for his great kindness in this matter, especially because he made it possible for me to examine the hearts from those dying suddenly from both natural as well as traumatic causes. I also wish to thank Prof. J. B. Herrick and Dr. Noel for aid in obtaining suitable hearts. The large majority of the specimens came from the dead-house of the Cook County Hospital.

As far as possible accurate observations were made in regard to the time of examination after death, to the degree of contraction and of fulness of the different cavities of the heart, and especially as to the looseness or firmness of texture of the heart's flesh, in order to obtain, if possible, any data that would warrant the formation of an opinion as to the presence of segmentation from the mere naked-eye inspection. In the majority of the cases teased preparations from the left papillary muscles and from the ventricular septum were made in physiological salt solution and mounted in glycerine. Taking the statements of Tedeschi and Oestreich for granted, namely, that if fragmentation is present at all in a heart, it will be found first in the left papillary muscles and then in the septum, it was concluded that if the teased specimens failed to demonstrate segmentation, then no further examination of such hearts would be made except to harden, embed, and make stained sections from the two places mentioned, in order to control the correctness of the conclusion based on the examination of the teased preparations. It was found that practically, without any exception, the study of carefully and gently made teased specimens will demonstrate satisfactorily the presence or absence of general segmentation. Small pieces in which the fibres run parallel with each other should be used and carefully dissociated by means of fine, clean needles. Teased specimens are hardly sufficient, however, to demonstrate the absence or presence of focal segmentation, because the routine histological examination of a number of specimens in which teasing had not revealed any changes showed frequent foci of segmentation. Whenever the teased specimens showed fragmentation, suitable pieces were cut out from the different parts of the hearts and hardened in 5 per cent. solution of formalin, in alcohol, or in Müller's fluid, embedded in celloidin or paraffin, and stained (after fixation on the slide in the case of paraffin specimens), mostly with hæmatoxylin and eosin. A few fatty degenerated hearts were fixed in Flemming's solution and stained with safranin. I can confirm Tedeschi's statement that none of the ordinary histological methods give rise to misleading artefacts. Like Tedeschi, I also observed that the intercellular cement becomes markedly prominent in preparations fixed in Flemming's solution; but inasmuch as it concerned mostly fatty hearts, usually with some real dissociation, I cannot say how much of the apparent change was real and how much artificial.

In the table showing the percentages I have included under the heading "Segmentation and Fragmentation," in addition to the typical cases, all the instances in which the intercellular substance was plainly visible in the teased specimens, because this change is undoubtedly closely related to actual segmentation, and also all cases of more or less well-marked fragmentation in which it seemed reasonable to believe that the change was not wholly an artefact.

TABLE SHOWING THE RELATIONS OF MYOCARDIAL DISUNION TO SEX AND AGE IN 190 CASES.

Decimal periods.	Normal.		Segmentation and fragmentation.		Percentage of disunion.	
	Female.	Male.	Female.	Male.	Female.	Male.
I.	5	9	1	0	16.66	0
II.	2	4	0	4	0	50
III.	4	9	8	22	66.66	70.96
IV.	3	14	9	19	75	57.57
V.	1	5	7	25	87.50	83.33
VI.	3	1	1	17	25	94.44
VII.	2	3	3	9	60	75
Total . . .	20	45	29	96	59.18	68.08

Total number of cases 190
Disunion in . . . . . 65.78 per ct.

THE FREQUENCY OF SEGMENTATION AND ITS RELATION TO OTHER DISEASES. (*a*) *General Frequency.* v. Recklinghausen[1] found segmentation present in all cases of spontaneous sudden death occurring in the course of chronic myocarditis, coronary sclerosis, or changes at the root of the aorta; in many acute infectious diseases; in cases of sudden death in nephritis with cardiac hypertrophy, but without cerebral hemorrhage; in rapid death from cerebral hemorrhage; and, finally, in many cases of sudden death due to traumatism and other causes. He did not find it in influenza or acute articular rheumatism.

Tedeschi[2] gives the following statistics: In two hundred and thirty-six cases of death from various diseases he observed segmentation or fragmentation in 48 per cent. (in the men 44 per cent., in the women 53 per cent.); twenty-three cases, from one to ten years old, gave 9 per cent.; twenty cases, from eleven to twenty, gave 50 per cent. (43 per cent. in the male and 66 per cent. in the female); fifty-seven cases, from twenty-one to thirty, gave 48 per cent. (43 per cent. in the male and 53 per cent. in the female); forty-eight cases, from thirty-one to forty, gave 54 per cent. (61 per cent. in the male and 45 per cent. in the female); thirty-one cases, from forty-one to fifty, gave 62 per cent. (44 per cent. in the male and 86 per cent. in the female); thirty-one cases, from fifty-one to sixty, gave 40 per cent. (equal in both sexes); fourteen cases, from sixty-one to seventy, gave 80 per cent. for men and 100 per cent. for

[1] Loc. cit.

[2] Loc. cit.

women; after seventy-six years, 50 per cent. for men and 33 per cent. for both sexes. As regards diseases, severe general infections in adults were accompanied with this lesion in 82 per cent.; deaths after severe operations in 100 per cent. (ten cases); cerebral diseases in adults in 92 per cent; heart-diseases in 50 per cent. of the cases.

Oestreich,[1] without presenting any figures, says that, after extended observations, it would be practically impossible to name a disease in connection with which he had not observed fragmentation—it may occur in every disease.

In one hundred and ninety consecutive cases that I have examined segmentation and fragmentation in the broadest sense occurred in 65.78 per cent. Except in the first, and, to a less extent, in the second, decennium, this lesion is certainly present in the majority of the cases that die from the ordinary causes under familiar circumstances. In about one-half of the cases it concerned a marked general dissociation.

In the first decennium the only instance in fourteen cases occurred in an eighteen-months-old girl that died from acute nephritis and bronchopneumonia. The cement substance was clearly visible, and there were a number of ruptured fibres. The other cases examined include a wide range of pathological conditions.

In the second decennium there were four instances of focal or slight segmentation in ten cases. Two were quick deaths from traumatic causes (crushing injury and bullet-wound of chest), one died from gas-asphyxia, one after a bullet-wound of the spleen, and all were free from any important chronic diseases.

(*b*) *Relation of Segmentation to Infections.* A general bacteriological examination was made in forty-nine cases. In fifteen the organs and the heart's blood were sterile; in thirty-four the commoner forms of bacteria (the colon bacterium, the pyogenic cocci, the micrococcus lanceolatus, the typhoid bacillus) were found more or less widely distributed. Segmentation and fragmentation were present in twenty of these cases and absent in fourteen. Without entering into details it may be said that any inseparable relation between any single micro-organism and segmentation in general, or at any particular period of life, could not be demonstrated from this small number. Thus, the colon bacillus was present in eight instances, four of which were cases of peritonitis; in three of the eight segmentation was present; the youngest of the five in which it was absent died at fifteen, the oldest at forty-five, both of peritonitis. In ten cases it concerned fatal infection with the micrococcus lanceolatus in the form of an anatomically typical lobar pneumonia frequently associated with endocarditis, pericarditis, and meningitis. In all these cases, the ages of which varied from twenty-three

[1] Loc. cit.

to sixty years, the heart was hypertrophied, weighing from 380 to 730 grammes, arterio-sclerosis being present in some of the hearts. Segmentation was present in nine. In eight cases of typical fibrinous pneumonia, but without bacteriological examination, disunion was observed five times.

In eleven cases in which the blood and the organs were sterile, dissociation was observed in five, including sarcomatosis, puerperal eclampsia, constitutional syphilis with interstitial nephritis, and glioma of the brain.

In two cases in particular there were found enormous numbers of rather long bacilli in the generally segmented heart-muscle, scattered between the sides and ends of the segments (Fig. 7). One was killed directly by a wagon passing over the abdomen, the other died instantaneously from the rupture of an aortic aneurism. This was, therefore, undoubtedly a post mortem bacillary invasion; and the possibility that the bacilli may have dissolved the cement substance cannot be wholly denied, although it must be remembered that segmentation is observed in cases of sudden traumatic death examined at once. It is evident, however, that the vital, agonal, or post-mortem action of bacteria upon the heart-muscle cannot account for the occurrence of segmentation and fragmentation in general.

(*c*) *The Relation of Segmentation to Diseases of the Heart.* While the number of cases from which deductions concerning the above question can be made is rather insufficient to warrant any extended analysis, yet the frequency with which segmentation occurs in connection with hypertrophy of the heart, due to the usual causes and often independent of the fatal disease, must be emphasized. Thus, in forty-three adult male cases the hearts of which weighed from 320 to 850 grammes, segmentation was present in 90 per cent.; in sixteen adult female cases in which the hearts weighed from 270 to 900 grammes, segmentation was found in 68.75 per cent.; or in fifty-nine cases of men and women with hypertrophy of the heart, fragmentation was present in 74.57 per cent. More or less extensive chronic fibrous changes, in the broad sense, were present in most of these hearts. In twenty-one adult cases of atrophy of the heart (in women less than 240 grammes, in the men less than 290 grammes) segmentation, often in slight degree, or merely in the form of visible cement line, was present in 57 per cent. In all these cases it concerns hearts that were actually weighed.

(*d*) *Relation of Segmentation to Sudden Traumatic Death.* In the list are ten cases of death due to traumatism, such as gunshot-wounds and crushing railroad injuries. In the majority death was practically instantaneous. In all some degree of segmentation was present. Two cases occurred in individuals less than twenty years old.

The Naked-eye Appearances of Hearts the Seat of Dissociation. In "typhoid" and "asthenic" conditions—in which disso-

ciation is so often present—the heart is usually more or less dilated and flaccid, its muscle reddish, brownish, or grayish-yellow, opaque, and friable or loose in its texture. These appearances, however, depend largely upon accompanying parenchymatous degenerations (*myodegeneratio cordis*). Segmentary dissociation may be present without marked changes in color and consistence. Focal segmentation in particular may be present in the firmly contracted hearts, and von Recklinghausen,[1] Langerhans,[2] and Oestreich[3] describe general segmentation in hearts that were not dilated. Renaut[4] urges the general diastole of dissociated hearts as evidence against segmentation being caused by irregular or violent agonal contractions or ultimate tetanization, as claimed by some, which should leave the heart—in persons examined immediately post mortem—in systole. Segmentation is frequently found in hypertrophic hearts that appear quite firm and contracted. Consequently, changes in color and in consistence, as determined by contraction or dilatation, are not necessarily indicative of dissociation. According to Kaufmann,[5] advanced segmentation may produce wavy swellings on the endocardial surface, especially on the papillary muscles. Oestreich[6] regards increased friability and looseness in texture as very important evidence of dissociation. If, on stroking the cut surface, especially where the fibres run parallel, gently with the knife, clefts and fissures appear numerously in the myocardium, segmentation is quite surely present, even though the heart as a whole may have been quite firm and contracted. This corresponds with my experience. Focal and slight separation, however, require microscopic examination for their demonstration; and in any event it would not be wholly reliable to base a positive diagnosis of general segmentation on the naked-eye appearances only.

The Histology of Segmentation and Fragmentation. Segmentation may present itself in varying degrees. In many hearts distinct, finer or broader, apparently swollen lines, often staining quite deeply with eosin, run transversely across the fibres at irregular intervals (Figs. 1 and 5). The lines may be straight or curved, which is usually the case, or crooked, zigzag, or step-like. Occasionally they extend wave-like through several adjacent and parallel fibres. When diastasis of the fibre has occurred, the substance forming these lines can often be recognized at one of the ends of the separating fibre, while the other end may be smooth or finely irregular or ragged. Incomplete separation along the cement lines is also occasionally observed.

In the twelve instances of this series in which the cement substance was plainly visible in the form of narrow or broader lines, while segmentation was not presented, it concerned in the majority of cases

[1] Loc. cit.
[2] Demonstration eines Falles von Carbolvergiftung, Berl. kl. Wochenschr., 1893, 37.
[3] Loc. cit.
[4] Loc. cit.
[5] Lehrbuch der sp. Path. Anat., 1896, p. 24.
[6] Loc. cit.

decidedly atrophic and pigmented or fattily degenerated hearts from adult persons dying from chronic tuberculosis (two), diabetes (one), and carcinoma (stomach, three; larynx, one), the heart in each case weighing less than normal and in one case only 125 grammes; but this condition was also observed in persons dying from peritonitis after bullet-wound (one), from sarcoma of the pons (one), from carbolic-acid poisoning (one), from cysto-uretero-pyelo-nephritis following rupture of the urethra (one), and from cerebral hemorrhage (one).

FIG. 1.

Cement lines visible. Man, aged sixty, carcinoma of stomach. × 125.

In quite a few cases typical segmentation producing larger or smaller segments with mostly clean-cut ends occurs in smaller or larger foci and not generally throughout the parts examined. In some of these specimens the cement lines are visible about the foci of dissociation (Fig. 2). Often a complete cell with its lateral branches is loosened. The width of the space separating the segments may vary considerably. (In some instances foci of segmentation were not found as usual in the left papillary muscles, but elsewhere in the left ventricle; but this was

the case only when there were extensive fibrous changes in the papillary muscles.) In some of these cases the heart is otherwise absolutely healthy. In some there are extensive fibrous changes; in some the nuclei are very large, and extensive fatty degeneration may be present. Occasional tears also occur.

From focal dissociation the process may be said to extend through transition stages of slight, then more and more pronounced separation, to well marked, general segmentation throughout the whole left ven-

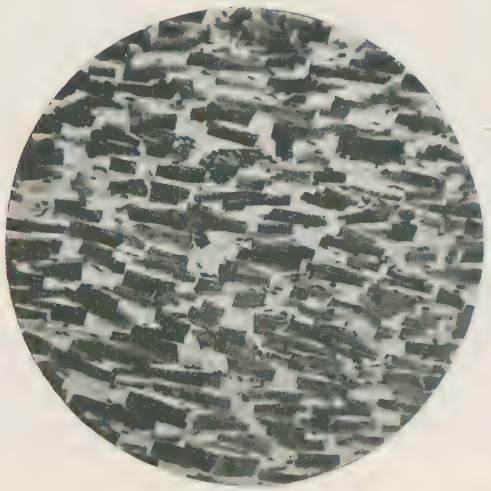
FIG. 2.

Cement broad; some segmentation and, in the centre, a segment partly broken across. Man, fifty-six, arterio-sclerosis, rupture of aneurism into pericardium; hypertrophy of heart. × 500.

tricle. In these instances of marked segmentation the change is also usually present in the right ventricle, and in this case it also occurs first and best marked in the papillary muscles. Segmentation is evidently very rarely present in the auricles. The marked frequency with which the papillary muscles are involved is attributed by Israel to absence of antagonistic diagonal fibres.

Typical segmentary dissociation gives rise to segments that correspond quite generally to the outlines of the muscle-cells isolated by means of solution of potassium hydrate. The ends may be straight, concave, or convex, dentated, or terraced, often finely irregular; lateral processes are present; larger segments, evidently composed of more than one cell, are also found; small square or oblong segments without nuclei, as well as irregular fragments, frequently occur, evidently due to the mechanical fracture of the lateral processes of the loosened segments, but fracture lines very rarely pass near the nucleus (Fig. 3). More or less diastasis of the segments has usually taken place, and the intervening spaces are oftenest apparently empty. Generally the separated pieces maintain a relatively normal position, but sometimes disarrangement has been brought about, due, it would seem, to the contraction of adjacent fibres after segmentation has occurred and to loosening of the interstitial tissues, allowing the bundles to become mixed (Israel[1]). In

FIG. 3.



Marked general segmentation with great diastasis of the pieces. × 120.

occasional cases extravasation of red blood-corpuscles has occurred between the ends of the segments—a fact emphasized by Browicz[2] and others in establishing the vital nature of segmentation. In the vicinity of inflammatory foci leucocytes are found between the ends of the pieces (Fig. 4), and in some cases of ante- or post-mortem bacterial invasion the spaces may be occupied by micro-organisms (Fig. 7). Generally the separation is complete. Occasionally, however, there are faint indications of the presence of a delicate membrane covering the fibre and still holding

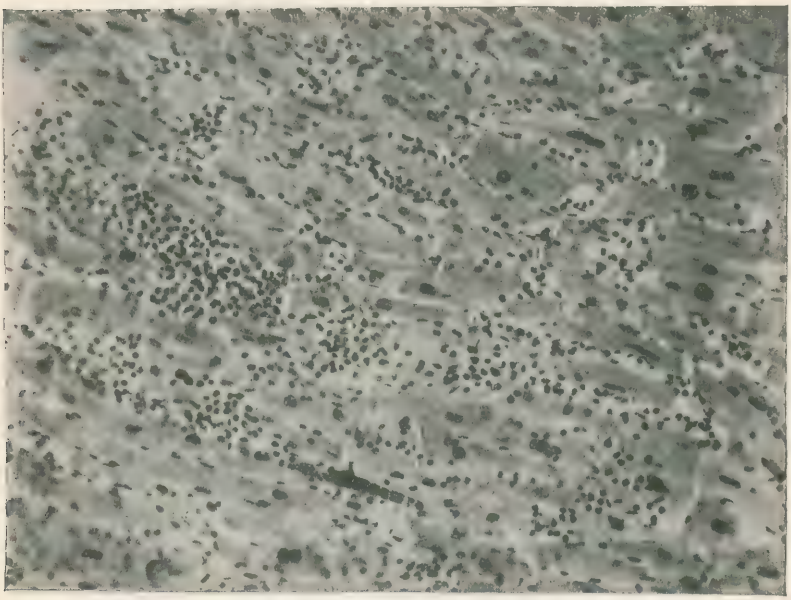
[1] Loc. cit.

[2] Loc. cit.

the ends together—a sarcolemma, the existence of which in the heart-muscle is, following Eberth,[1] usually denied. Oestreich[2] also notes having observed this delicate membrane. Perhaps the connective-tissue fibrillæ become closely applied to the separating muscle-fibres and give rise to the appearance of a sarcolemma.

Otherwise the section of the heart-muscle may appear perfectly normal, the striations being distinct, the nucleus of usual size, the connective tissue and bloodvessels unchanged. In many cases the general loosening of the secondary bundles described by Israel is present; or there may be, depending upon general conditions, such as infections and intoxi-

FIG. 4.



Acute interstitial myocarditis in pyæmia. Near lower margin a compact micrococcal embolus (staphyloc. pyog. aur.). Leucocytic infiltration, segmentation, leucocytes between the pieces. × 500.

cations, parenchymatous and fatty degenerations (Fig. 5) of the sarcoplasma as well as the changes usually included under the term chronic fibrous myocarditis. In a large number of the cases, particularly in hypertrophy of the heart, with or without chronic myocardial changes, there is noted marked increase in the size and changes in the shape of the nuclei of the muscle-cells. The nuclei may indeed be giants in size. In shape they may be greatly elongated and cylindrical or spread out in

[1] Loc. cit.

[2] Loc. cit.

the form of oval masses; club-shaped, kidney-shaped nuclei, and nuclei with budding processes and curiously shaped outgrowths also occur; some are vesicular, others stain very deeply, and sometimes they present surface markings, due probably to the imprints of pressure, which may give the nucleus an appearance as though it were to split longitudinally (Fig. 6).

Fragmentation, tearing, or breaking of the muscle-fibres, usually present to some extent in all cases of marked segmentary dissociation, as shown by the presence of small fragments often without nuclei, in some cases occurs to a more marked extent, and may be the predominating form of disunion. The lines of separation may pass through any part of the muscle-cell, often passing around one pole of the nucleus, the margins or ends of fragments being more irregularly ragged than in segmentary dissociation. Incomplete rupture may occur. Fragmentation, strictly speaking, never occurs to such an extent and does not give rise to separation into such minute pieces as does segmentation. It appears to bear the same general relations to acute and chronic diseases as segmentation, and in agreement with Bard, Renaut, and others the conclusion seems warranted that it is caused largely by mechanical rupture or breaking of the fibres on account of various degenerative changes that render the sarcoplasm brittle.

FIG. 5.

Cement lines broad and visible in a heart the seat of fatty degeneration. × 500.

THE DISTINCTION BETWEEN SEGMENTATION AND FRAGMENTATION. In the foregoing the attempt has been made to consistently employ the words segmentation or segmentary dissociation and fragmentation to designate two distinct conditions, each in the main well described by the term applied to it—segmentation referring to the division of the muscle-cells at the lines of junction in the muscle-fibre, fragmentation to the rupture or break of the fibre regardless of the cement lines.

While Renaut[1] and his pupils, Browicz[2] and others, insist that the interruption of the continuity of the cardiac muscle-fibres that gives rise to the characteristic appearances described by them as *myocardite*

FIG. 6.

Cylindrical and peculiarly shaped giant nuclei; in the centre a cell with vacuolar degeneration of its protoplasm. Man, age fifty, heart weighed 700 gr., fibro-myocarditis. × 500.

segmentaire occurs principally along the lines of union between the single muscle-cells, others claim that the lesion is produced essentially by ruptures or breaks of the muscle-fibres without any special reference to the limits of the individual cells.

Browicz regards all interpretations of segmentation that do not make the limits of the pieces correspond with the limits of the cells as erroneous. He does not lay so much stress on the mere dissociation of the muscle-cells, which probably is an agonal product, as upon vital patho-

[1] Loc. cit.

[2] Loc. cit.

logical conditions of the intercellular substance, manifesting itself by the fact that the lines of junction become visible. It may be a homogeneous seam, a broad stripe, or a broader layer whose contours are sharply separated from the ends of the cell. In this space are then found short, stave-like formations running parallel to the long axis of the muscle-fibre ("*breitstreifige, stäbchenformig gebaute Kittsubstanz*"), and such changes may alternate with distinct dissociation. In this statement Browicz has been in a measure substantiated by Przewoski's[1] investigations, which show by special methods that at the ends each muscle-cell has a layer of granules, the *stratum granulosum terminale.* Browicz looks upon these changes in the cement as the initial phase of segmentation.

Eberth[2] long ago called attention to the fact that in atrophic and pigmented hearts the fibres may separate into single cells without any manipulations, and he ascribes this dissociation to fragility of the cement.

Goebel[3] also regards segmentation as beginning with changes in the intercellular cement, and the separation as occurring at the lines of union between the cells.

v. Recklinghausen,[4] Marchand,[5] Oestreich,[6] and Bard[7] lay stress upon the rupture of muscle-fibres as an important step in producing the *état segmentaire* of Renaut. In fact, the last two regard multiple ruptures as the essential occurrence. It concerns fragmentation in the strict sense, and not segmentation, and the process does not depend upon changes in the cement substance (v. Recklinghausen[8]). Oestreich[9] found that some of the fragments were so small that they could not possibly be whole cells. Furthermore, that the lines of rupture very often passed across the fibre in the immediate neighborhood of the nucleus, and sometimes in a curve around one pole of the nucleus, half of which would then project into the indentation of the corresponding fragment. He also found that the fragments were more like the artificial muscular bits described by Eberth than like isolated muscle-cells. Finally, he was able by means of the action of acetic acid to demonstrate the presence of unchanged cement lines near rupture lines. Often the rupture would pass across the fibre near the unchanged lines of union.

While Oestreich[10] is surely correct in the statement that many fragments are too minute to represent whole cells—fragments without nuclei also occur—as well as in the observation that rupture lines often pass immediately around the nucleus, I have not been able to confirm the statement that the fragments generally resemble artificially produced

[1] Cited by Browicz, loc. cit. [2] Loc. cit.
[3] Beiträge zur fettigen Degeneration des Herzens, Centralb. f. Allg. Path. u. Path. Anat., 1893, Bd. iv. p. 728.
[4] Loc. cit. [5] Loc. cit. [6] Loc. cit. [7] Loc. cit.
[8] Loc. cit. [9] Loc. cit. [10] Loc. cit.

muscle-morsels nor to demonstrate by addition of acetic acid normal cement lines in all hearts the seat of marked dissociation. Eberth[1] describes artificial muscular detritus as presenting more clean-cut and more nearly straight ends than the isolated muscle-cells, the ends of which are usually finely irregular, while occasional fibrillæ may project from the ends of forcibly produced fragments, yet the ends of the fibrillæ are not pointed, but cut off squarely. Oestreich uses this statement as a standard in distinguishing between segmentation and fragmentation in human hearts. When making the statement Eberth[2] does not refer to any special species, but to normal heart-muscle in general. Segmentation is a morbid process. There is, therefore, no inherent reason why it may not cause disunion of the muscle-cells and yet the ends be square and clean-cut. For these reasons no weight can be given the conclusions drawn by Oestreich after comparing the segments of dissociation with the artificial fragments described by Eberth.

Histologists—as, for instance, Schweigger-Seidel, in Stricker's *Handbook*—also describe normal muscle-cells with smooth ends, and believe the difference in the limiting surfaces to be occasioned by the circumstance that the muscle sometimes comes under observation in a contracted, coagulated condition. I think it will be found that the ends of fragments of the normal human heart produced by force, pressure, tearing, bending, which I presume is what is meant when Eberth speaks of "artificially produced muscular detritus," are strikingly ragged and irregular, the fibrillæ yielding unequally. Furthermore, in typical, general, marked segmentation, such as is shown in Fig. 3, it is not generally possible to demonstrate any cement lines. On the other hand, the outlines of the segments correspond very nicely to the shape and the size of the isolated muscle-cell, which, forsooth, they often are; nor is it usual to find in such specimens that a line of separation crosses a segment in the region of a nucleus. The study of cases of focal or slight dissociation will also be found to substantiate quite fully the statements of Browicz[3] in regard to the coexistence of visible cement lines and actual segmentation. On the other hand, fragmentation in the strict sense also occurs, as acknowledged by Renaut,[4] although probably not to the extent claimed by Oestreich,[5] and here the ruptures very often cross the fibres near the nucleus, and hence probably inside the limits of the single muscle-cells. The nucleus, however, is not always central. It may be found quite near one end of the cell. In many specimens it is also possible to demonstrate the coexistence of cement lines independent of the fracture lines, the ends on each side of the latter being usually very irregular and ragged, as if the fibre had been torn forcibly across, the fibrillæ offering unequal resistance.

[1] Loc. cit. [2] Loc. cit. [3] Loc. cit. [4] Loc. cit. [5] Loc. cit.

The conclusion is therefore in order that segmentary dissociation as well as actual fragmentation or rupture of the fibres of the heart-muscle both occur.

Distinction should be made between typical segmentary dissociation of the heart muscle-fibres, in which softening or complete solution or perhaps excessive brittleness of the cement allows the muscle-cells and segments to move away from each other, and fragmentation in the strict sense of the word, it which it essentially concerns ruptures of the muscle-fibres in any part of their course and without any special reference to the lines of union. This distinction is quite important, because the possibility that fragmentation may be, to a certain and perhaps large extent, artificial, cannot be altogether excluded, while segmentation cannot be produced by the action of ordinary reagents and manipulations. For these reasons I have preferred to deal more with segmentation than with fragmentation. Segmentation and fragmentation frequently occur in varying degrees. In any large series of hearts it will be found that it is quite feasible to separate the specimens into two groups, according as one or the other of these forms of interruption in the continuity of the muscle-fibres predominate; but true segmentation is by far the more frequent.

The Causes, Nature, and Clinical Significance of Segmentation. The views concerning the nature and the cause of segmentary dissociation have, as noticed, failed to harmonize. It was the earlier belief of Renaut[3] that it concerned a primary, nutritive, or chemical change of the cement substance. This view has been supported by his pupils, by Browicz,[1] v. Zenker,[2] Tedeschi,[3] and in part by Israel[4] and Dunin.[5]

Durand[6] and Duplaix[7] claimed that in circulatory disturbances more or less permanent œdema of the myocardium may be produced, and the substances contained in the œdematous fluid, such as sarcolactic acid, may dissolve the cement, holding the muscle-cells together in the form of muscle-fibres. Durand[8] calls attention to the direct action of very feeble solutions of chromic and other acids upon the cement; but Colrat[9] produced œdema of the heart experimentally without the occurrence of segmentation. Segmentation also occurs in many conditions, such as atrophy of the heart, sudden traumatic death, etc., without the presence of œdema.

v. Recklinghausen,[10] Oestreich, and Rosenbach[11] look upon the change more as a mechanical disunion and rupture of the muscle-fibres on account of disturbances of innervation and irregular contraction in the death agony, favored perhaps by brittleness of the fibres due to degen-

[1] Loc. cit. [2] Loc. cit. [3] Loc. cit. [4] Loc. cit.
[5] Loc. cit. [6] Loc. cit. [7] Loc. cit. [8] Loc. cit.
[9] Loc. cit. [10] Loc. cit. [11] Loc. cit.

erative changes. Oestreich[1] says fragmentation does not cause death but the last contraction causes fragmentation. Rosenbach[2] states that a maximal contraction precedes dissociation, and that it may be regarded as proved that it is due to the crossing of impulses of different nature in a dying heart. When an impulse of excitation meets an inhibitory impulse, separation of the fibre occurs. Letulle[3] expresses the opinion that segmentary dissociation is due to an agonal imbibition of the muscular fibres with sarcolactic acid. Finally Renaut,[4] in his efforts to overthrow v. Recklinghausen's[5] and Ostreich's[6] views concerning the essentially agonal nature of segmentation, advances the claim that it is the last step of a complex, dystrophic, cellular process, involving the muscle-cells and leading to softening and solution of the intercellular substance.

Lepine and Molard,[7] in 1891, described certain degenerative changes in the heart muscle-fibres as a particular species of non-sclerotic, parenchymatous myocarditis. The changes consist in the appearance of clear spaces between the primitive fibrillæ, which are thereby forced apart. These spaces are largest near and about the nucleus, which is increased in volume, round, ovoid, or elongated. In consequence of these conditions the fibres, when cut longitudinally, present a bulging enlargement corresponding mainly to the situation of the nucleus. The heart that is described as presenting these changes in typical form weighed 560 grammes, was dilated, and came from a man seventy-eight years old. Segmentation and other lesions are described as absent. Subsequently, however, Renaut, in 1894, calls attention to the fact that segmentation was present in all of Lepine's and Molard's preparations, and, based on further studies, he makes the hyperplasmic atrophy or vacuolar disintegration and gigantism of the nuclei, described by these authors, steps in a complex process leading to segmentation. The enlargement of the nucleus, the increase of the amount of the chromatin, are interpreted by Renaut as evidences of augmented nuclear activity, the muscle-segment assuming, as it were, a more intense "nuclear life," while its function and its structure as a contractile element fall into abeyance, and the intercontractile substance is liquefied. *La cellule vit dès lors bien plus cellulairement que musculairement.* Finally the cell softens or dissolves its cement, which may swell up and become permeable to the corpuscles of the blood and the lymph. The muscle-cell is now functionally incapacitated, and general segmentation is the anatomical sign and final lesion of cardiac asthenia. The "hyperplasmic atrophy" of Renaut, as well as the special form of parenchymatous myocarditis of

[1] Loc. cit. [2] Loc. cit.

[3] Anatomie Pathologique (Cœur, Vaisseaux, Poumon), Paris, 1897.

[4] Loc. cit. [5] Loc. cit. [6] Loc. cit.

[7] Sur une espèce particulière de myocardite parenchymateuse (sans sclérose), Arch. de Méd Expérim., 1891, p. 777.

Lepine and Molard,[1] would seem to correspond very closely to vacuolar degeneration of the muscle-fibres (Figs. 6 and 7), which is due to a colliquative disintegration of the sarcoplasm. It is often associated with enlargement or vesicular tumefaction of the nuclei, and is generally observed in connection with interferences of the coronary circulation (Letulle[2]), and occurs probably also in diverse general intoxications. This condition may or may not be associated with segmentation. Incidentally attention may be called to the fact that spaces in the muscle-fibres of the heart very much similar to these vacuoles have been interpreted as capillaries within the muscle-fibres by Meigs.[3]

Fig. 7.

Segmentation; bacilli upon and between the segments; to the left of the centre a cell with vacuolar degeneration and containing two nuclei. Man, fifty, died instantly from crushing injury of abdomen. × 500.

Segmentation occurs frequently in association with hypertrophy of the heart, with or without degeneration. Here, also, enlargement of the nuclei, which may assume various shapes, is, as a rule, present. Letulle[4] states that every muscular fibre that hypertrophies presents a proportional enlargement of the nucleus; and Tangl,[5] who made his observations upon the left ventricle of the hearts of rabbits, the hypertrophy

[1] Loc cit. [2] Loc. cit.

[3] The Microscopic Anatomy of the Human Heart, Transactions of the College of Physicians of Philadelphia, 1891; and The American Journal of the Medical Sciences, 1891.

[4] Loc. cit.

[5] Ueber die Hypertrophie und das physiol. Wachsthum des Herzens, Virch. Arch., 1889, Bd. cxvi. p. 432.

being secondary to experimental traumatic lesions of the aortic valve, found the nuclei of the hypertrophic cells of varying shape, mostly oval, sometimes with central constrictions. Often the nuclei were very long, and they seemed in general to enlarge with the cells. Furthermore, the nuclei were surrounded by a granular substance that coalesced with the protoplasm of the periphery of the cell in which small vacuoles were occasionally seen. Evidently the enlargement of the nuclei and their richness in chromatin in purely hypertrophic hearts belong to the hypertrophic process, and cannot in general be assumed to be evidence of any "dystrophy" leading to segmentation. According to Tangl, it is not entirely impossible but that vacuolation of the sarcoplasm may also occur in pure hypertrophy.

Finally, it must be borne in mind that segmentation occurs without "hyperplasmic atrophy" and "gigantism of the nuclei," as witness segmentary dissociation of healthy hearts in connection with sudden, traumatic death, as well as in other conditions. Hence Renaût's claim that segmentation depends upon the existence of a special dystrophic process of the myocardium proper, marked by vacuolar changes in sarcoplasm, by gigantism of the nuclei, and by solution of the cement, is to be regarded as rather broad, first, because segmentation occurs in otherwise healthy heart-muscle; second, because although segmentation occurs generally in hypertrophic hearts, often with secondary degenerative changes, yet it has not been demonstrated that the enlargement of the nuclei observed in such heart-muscle is always dystrophic or degenerative, and not to a large extent progressive and hypertrophic in its nature. The entity of Renaut's dystrophic process is, therefore, still questionable.

Segmentary dissociation occurs so frequently in connection with various acute and chronic myocardial changes as to warrant the conclusion that the cement substance may be altered, softened, or rendered brittle by direct action of general conditions as well as indirectly on account of primary or secondary lesions of the muscle-cells. Broad, visible cement layers, focal segmentation, segmentation confined to districts of fatty degeneration in the heart-muscle, dissociation about acute myocarditic foci with leucocytes between the segments, the limited segmentation that occurred around Tedeschi's[1] aseptic wounds of the heart, all point in this direction. Consequently it would seem that v. Recklinghausen's claim that it is not shown that segmentation can occur before the death agony no longer holds good.

It stands to reason that the changes in the muscle-cells must influence the quality of the cement. This seems actually demonstrated in the following case, instances similar to which I could duplicate:

[1] Loc. cit.

Ambrosius[1] details the case of a woman, aged forty years, who died ninety hours after the removal of the tubes and ovaries under chloroform. There were fatty degeneration and exquisite segmentation of the heart muscle with vesicular nuclei. The degree of fatty degeneration corresponded nicely to the limits of the different degrees of segmentation, pointing to the presence of a vital, histological variation in the different fibres, and permitting the inference that dissociation occurs in places prepared for it by changes in the muscular tissue.

As the cement becomes changed focal and general dissociation may occur under normal or abnormal conditions of cardiac activity. Diastasis and disarrangement of the pieces may follow in degrees commensurate with the vigor and the irregularity of the contractions. The coexisting brittleness of the sarcoplasm and presence of loosened segments between still contracting muscular bundles may lead to more or less extensive fragmentation. The conditions present in diseased and especially in hypertrophic hearts favor dissociation. Here are lesions of various kinds of the muscle-cells, of the stroma, and of the blood-vessels that may weaken the cement and the plasma of the cells, and also marked disturbances in the vigor and order of the contractions. It is certainly difficult to account satisfactorily for segmentation in cases of traumatic, sudden death in which the heart-muscle is plainly normal in its structure. In general it may be assumed, however, that dissociation of the muscle-fibres results from a disproportion between the vigor of the muscular contractions and the muscular cohesion. Segmentation and fragmentation may, therefore, occur in normal heart-muscle if its contractions be excessively violent and irregular, as may be the case, for instance, in hanging, in sudden *exitus letalis* during coitus, in excited states, in delirium, etc., and thus become the immediate cause of death because the heart can then no longer contract. In weakened hearts, violent or irregular as well as quite normal contractions may cause dissociation, suspending further cardiac action ; but this cannot be designated a true agonal change in the ordinary sense conveyed by this term.

The views as to the existence of segmentation in a form susceptible of clinical recognition (segmentary myocarditis of Renaut) are divided. Renaut and his scholars claim that in the old the condition occurs in such a typical form that it may be diagnosed, and that it should therefore be regarded as a clinical entity. This view has not gained general acceptance. Primary, independent segmentation is not yet recognized. Aufrecht,[2] in a short article, champions its existence.

[1] Ein Fall von spät eingetretenen Tod nach Chloroforminhalation nebst Bemerkungen zur Fragmentatio Myocardii, Virch. Arch., Supplementheft, 1895, Bd. cxxxviii.

[2] Ueber einen Fall von primärer Fragmentation des linken Ventrikel, Zeitschr. f. kl. Med. 1894, Bd. xxiv. p. 205.

Aufrecht describes a case in a man, forty-eight years of age, who died from the general symptoms of heart-failure, with œdema of the lower extremities. In the left ventricle there was universal segmentation, with hemorrhage between the segments, which are stated to have been normal with but occasional cloudiness. There was some hypertrophy of the right ventricle, which he interprets as secondary to the segmentation in the left, although the influence of a moderately marked pulmonary emphysema cannot be excluded.

Aufrecht regards this case as one of primary, independent segmentation of the left ventricle. There exists no ground, he claims, for not believing that a dissociated heart may not work as long as one the seat of parenchymatous degeneration. The muscle-fibres might undergo separation little by little, and the process need not necessarily coincide with the agony.

All the other authors regard general and focal segmentation as an accidental or secondary phenomenon occurring in the course of infections and intoxications in connection with the primary and secondary lesions of asystolic hearts, and with fatal traumatism. It constitutes, as is also shown by the statistics brought forward in this paper, an episode in the course of the principal affection. While it possesses an anatomical individuality, it is so common that it would be difficult to say in what disease it would surely be absent after, say, the twentieth year, and it would take a very long time to enumerate all the diseases in which it has been found present. Its presence may explain this or that detail in the clinical course of a number of processes, such as the termination by sudden death; but it is secondary, it is not a disease in the strict sense any more than cloudy swelling, for instance, and cannot, therefore, be considered as entitled to a place in our nosology.

General segmentation is inconsistent with the continuance of the heart's action. Its presence in cases of arterio-sclerosis, coronary disease, fibrous myocarditis, etc., that die suddenly, is consequently a satisfactory anatomical reason for the sudden fatal ending. In medico-legal practice cases of sudden death under more or less suspicious circumstances, or without any apparent cause, occasionally occur in which the most careful post-mortem fails to reveal any other explanation of death than general myocardial segmentation, as, for instance, in this example:

An apparently healthy man, twenty-three years of age, was "fooling" with two friends. Two hats were knocked off, and, as one of the men picked up his hat, he observed that his friend—the dead man—had fallen to the floor unnoticed. It was thought that he was shamming, but after waiting three or four minutes it was found that he was dead. At the post-mortem, ten hours after death, and made by Dr. Louis J. Mitchell, all the organs, including the brain, were macroscopically normal. The heart, especially the left ventricle, was flabby and dilated.

Microscopic examination showed the heart—unfortunately this was the only organ that could be examined—the seat of a general and typical segmentation.

In this case there is not much doubt that the extensive dissociation caused death, but the cause of the dissociation is not clear.

Ramond[1] reports the case of a thirty-year-old professional runner who fell ill after a run of thirty kilometres on a hot July day. There were fever, dyspnœa, *delirium cordis*, and anuria, death ensuing in a few hours. The post-mortem showed hyperæmia of all the organs and a flaccid, dilated heart. Microscopic examination showed absence of myocarditis, but a marked general segmentation and fragmentation of the fibres, with much extravasated blood. The nuclei stained well, and the transverse striæ were distinct. Ramond regards toxins due to muscular overexertion as the cause of the lesions.

While general fragmentation is obviously inconsistent with continued heart's action, focal segmentation need not, it would seem, of necessity, result in death. Browicz concluded that general segmentation leads to sudden death, but focal to cardiac insufficiency, or, possibly, to rupture of the heart or to fibrous substitution of the separated muscle-cells. The last two conclusions he states he is unable to substantiate.

Robin[2] found segmentation along the margins of the ruptures in two hearts in which were also endo- and peri-arterial changes. He looks upon the segmentation as the essential cause. Tedeschi[3] examined the muscle in the vicinity of the ruptures in two hearts. In one instance there were found chronic fibrous interstitial changes as well as scattered foci of fragmentation. In the second case there were no fibrous changes about the point of rupture, but blood-corpuscles were present between the isolated, single muscle-cells. Subsequently Tedeschi had opportunity to examine three additional museum specimens of spontaneous heart rupture, with, he states, the same result as in the last case above. From these results it would seem that, while complete details are not at hand, still, in some cases, segmentation and spontaneous heart rupture stand in such very close relation to each other that the question merits further study.

Of all the parts of the heart, segmentation occurs most frequently in the papillary muscles of the left ventricle. It is often present in a marked degree in these muscles only. If it occur some time before death, the result might be mitral regurgitation, taking it for granted that a dissociated papillary muscle is incapable of contraction, because physiologists in general agree (Landois and Sterling, Curtis, in *The American Text-book*) that it is the function of these muscles, by their

[1] Dissociation segment. du myocard dans un cas de cœur forcé, Bullet. et mem. Soc. Méd. 1896; abstracted in Centralbl. f. Allg. Path. u. Path. Anat., 1897, viii. p. 236.

[2] Loc. cit.

[3] Loc. cit.

contraction during ventricular systole, to hold the mitral valves taut and thus compensate for the narrowing of the cavity of the ventricle. Mitral regurgitation induced in this way may account in some degree for the marked pulmonary congestion so frequently present in cases associated with myocardial segmentation.

If it be assumed that segmentation may occur in foci some time before death, several important questions arise concerning the fate of the loosened cells. Of course the isolated, non-nucleated protoplasmic masses that are often split loose could not maintain their vitality. On the other hand, would the nucleated but dissociated cells necessarily die and become replaced by fibrous tissue? Is the vitality of the muscle-cell dependent upon the integrity of its cement? Could a reunion of the isolated muscle-cells by means of new cement occur? These are questions that cannot be answered at this time. Koester[1] remarks that the yellow degeneration (*enartung*) which is followed by scar-formation in the myocardium does not, in slight degrees, differ to any extent from the segmentary myocarditis of Renaut. I have studied carefully the appearance of the muscle-fibres in and about myocardial scars, and it has seemed that the fibres, generally speaking, undergo atrophy without segmentation. Segmentation rarely occurs in the muscle-fibres embedded in scars. Any evidences of replacement of muscle-segments by fibrous tissue were not found. It therefore appears reasonable for the present, in view of the uniform absence of any evidence of reactionary changes, to regard even focal segmentation as at the most a product of limited ante-mortem duration. In conclusion the facts brought forward may be summarized as follows:

The cardiac muscle-fibres frequently separate into muscle-cells and irregular fragments. Segmentation and fragmentation are due to disproportion between the vigor and order of muscular contraction and muscular cohesion. They occur in normal heart-muscle due to excessively vigorous and irregular contractions. More frequently they are encountered in association with acute and chronic, secondary, and primary myocardial changes that alter the cement, weaken the plasma, and predispose to dissociation under normal or increased heart's action. General segmentation is of brief duration, because its occurrence is incompatible with further cardiac contractions. Focal or limited segmentation may, perhaps, cause incompetency of the auriculo-ventricular valves, especially the mitral. It may lead to cardiac insufficiency, and, possibly, to rupture of the heart. The fate of loosened muscle-cells is not known. It seems, however, that focal dissociation is of but short ante-mortem duration. The occurrence of primary segmentation as a distinct disease is not proven.

[1] Verh. d. X. Intern. Med. Congr., Berlin, 1890, Bd. ii. Abth. ii.

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